UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,726	04/08/2004	Michael Wayne Graham	0763/74768-AAA/JPW/GJG/JR	1523

23432 7590 03/22/2011

COOPER & DUNHAM, LLP
30 Rockefeller Plaza
20th Floor
NEW YORK, NY 10112

EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
03/22/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,726	GRAHAM ET AL.	
	Examiner	Art Unit	
	BRIAN WHITEMAN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *158-202* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *158-202* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/15/10,1/6/11,5/8/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/15/10 has been entered.

Information Disclosure Statement

The provisional applications and US application and other documents cited in the information disclosure statement filed 5/8/09 and 12/15/10 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the provisional and US applications do not have a publication date and other documents were already cited in a previous 1449. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Several references (27, 28, 32, 46, 56-59, 61-65, and 78) cited in the information disclosure statement filed 12/15/10 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. These references are located in the instant application and are not relied on for an earlier effective filing date under 35 USC 120.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 158-162, 172-177, 183, 187-192, 198, and 202 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (US 6,506,559, of record)

The claimed invention reads on making and using a double stranded DNA construct comprising a first nucleotide sequence that is identical to a target gene, a second nucleotide sequence that is identical to the first nucleotide and placed in inverted orientation compared to the first nucleotide sequence, a stuffer which separates and links the first and second nucleotide sequence, a promoter and transcription termination sequence, wherein all of the sequences are operably linked together. The construct reads on a hairpin element when the construct is expressed in a cell because the two sequences when expressed would result in making the hairpin. When two identical sequences in a DNA construct are expressed and one sequence is placed in inverted orientation that resultant product is a sequence with a hairpin structure. Thus, a region of the nucleotide sequence in the construct would be the loop segment of the resultant product with a hairpin structure and read on the stuffer fragment of the claimed construct.

Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 7-9). Fire teaches that the dsRNA construct is an improvement over antisense, ribozyme technology used for inhibiting a target gene (columns 1-3). Fire teaches at least one strand is produced by transcription of an expression construct (columns 7-9 and 28). The construct comprises a regulatory region (e.g., promoter, enhancer. polyadenylation) and use to transcribe the RNA strand(s) (columns 8-9). The nucleotide sequence may be at least 25, 50, 100, 200, 300, or 400 nucleotides (column 8). Fire further teaches that a double stranded structure may be formed by either a single self-complementary RNA strand or two complementary strands (columns 4 and 7-9). In order to make the single self-complementary RNA strand, the skilled artisan would have to make a construct comprising two identical sequences, wherein the second sequence is placed in an inverted orientation to the first sequence. The resulting single self-complementary RNA strand would contain a hairpin structure comprising a loop. The loop is considered to be a "stuffer" sequence because a certain number of nucleotides of the construct would have to form the loop. The teaching of Fire et al. embrace self-complementary RNA strands of greater than 400 bases, e.g., 25 consecutive nucleotides were identical to a sequence of a region of a target gene and another 25 consecutive nucleotides were complementarity. In such a molecule, an arbitrary number of nucleotides associated with the inherent hairpin region of the RNA strand can be arbitrarily considered to be a stuffer fragment that links 25 complementary base pairs. The vector can be introduced

into a cell, including cells find in humans (column 9-10). A viral vector can be used as the vector (column 9). The target gene can be a gene expressed by a virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made in view of Fire, namely to produce and use the construct further comprising a third and fourth structural gene. One of ordinary skill in the art would have been motivated to combine the teaching to study to see whether or not there is an additive effect of the combination.

Applicant's arguments, see pages 14-15, filed 12/15/10, with respect to the rejection(s) of claim(s) 134-147 and 150-155 under 103(a) have been fully considered and are persuasive because the claims were cancelled. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the addition of new claims.

Claims 163-168, 178-182, 191, and 193-197 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. as applied to claims 158-162, 172-177, 183, 187-192, 198, and 202 above, and further in view of Cowsert et al. (US 5,580,767, of record).

Fire et al. do not specifically teach a target gene selected from viral DNA polymerase, viral RNA polymerase, or a viral coat protein. NOTE: the provisional application for '559 discloses a target gene may be selected which is required for initiation of the disease or pathology.

At the time the invention was made, Cowsert teaches an oligonucleotide for inhibiting RNA polymerase to reduce the proliferation of a virus (column 3). It is acknowledged that Cowsert is directed to making and using a nucleic acid inhibitor possibly with a different mechanism of inhibiting/reducing expression of a gene, then the mechanism for dsRNA as contemplated by Fire et al. Fire et al. teach that dsRNA is an improvement over other nucleic acid inhibitors. Thus, one of ordinary skill in the art would have been obvious to try using the target gene for other nucleic acid inhibitors and studying whether there is an improvement using dsRNA compared to known nucleic acid inhibitor against the target gene.

In addition, at the time the invention was made, viral DNA polymerase and viral coat proteins were known for initiation of the disease or pathology of a virus. This would lead one of ordinary skill in the art to select a target gene selected from a viral pathogen, e.g., virus comprising a viral DNA polymerase, viral RNA polymerase, or a viral coat protein because these genes are required for initiation of pathology. Thus, one of ordinary skill in the art could make a construct comprising a nucleotide sequence targeting expression of a viral polymerase with a reasonable expectation of success.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire et al. taken with Cowsert et al., namely to produce and use the claimed product. One of ordinary skill in the art would have been motivated to combine the teaching to study the inhibition of expression of a viral RNA polymerase of a virus in a mammalian cell infected with the virus and/or if it is more efficient than antisense oligonucleotides at inhibiting expression

of a viral RNA polymerase. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See ***KSR v. Teleflex***, 550 U.S. 398, 127 S. Ct. 1727 (2007).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of a lentivirus. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of an immunodeficiency virus. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of a virus, wherein the gene is in an exon. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus by targeting the exon.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Cowsert, namely to produce an isolated mammalian cell comprising liposome or viral particle comprising a construct comprising a structural gene encoding RNA polymerase of a virus. One of ordinary skill in the art would have been motivated to combine the teaching since both are commonly used by one of ordinary skill in the art to successfully deliver a nucleic acid to a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 158-202 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 7,754,697 (of record) in view of Cowsert et al. (US 5,580,767, of record). Claims 1 and 2 of '697 recite:

> 1. A double-stranded synthetic DNA gene, comprising multiple copies of a structural gene region, wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in a eukaryotic cell, wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell, wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence, and wherein the structural gene region placed in the sense orientation and the structural gene region placed in the antisense orientation are separated by a sequence of nucleotides that is 50-100 nucleotides in length or 100-500 nucleotides in length.
>
> 2. The double-stranded synthetic DNA gene of claim 1, wherein the target gene is from a viral pathogen of a vertebrate animal cell.

The claims of '697 also recite an animal cell comprising the construct and method of using the construct.

However, the claims of '697 do not specifically teach a target gene selected from viral DNA polymerase, viral RNA polymerase, or a viral coat protein.

At the time the invention was made, Cowsert teaches an oligonucleotide for inhibiting RNA polymerase to reduce the proliferation of a virus (column 3). It is acknowledged that Cowsert is directed to making and using a nucleic acid inhibitor possibly with a different mechanism of inhibiting/reducing expression of a gene, then the mechanism for double stranded construct as claimed by Graham et al. Thus, one of ordinary skill in the art would have been obvious to try using the target gene for other nucleic acid inhibitors and studying whether there is an improvement using dsRNA compared to known nucleic acid inhibitor against the target gene.

In addition, at the time the invention was made, viral DNA polymerase and viral coat proteins were known to one of ordinary skill in the art for initiation of the disease or pathology of a virus. This would lead one of ordinary skill in the art to select a target gene selected from a viral pathogen, e.g., virus comprising a viral DNA polymerase, viral RNA polymerase, or a viral coat protein because these genes are required for initiation of pathology. Thus, one of ordinary skill in the art could make a construct comprising a nucleotide sequence targeting expression of a viral polymerase with a reasonable expectation of success.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of the claims of '697 taken with Cowsert et al., namely to produce and use the claimed product. One of ordinary skill in the art would have been motivated to combine the teaching to study the inhibition of expression of a viral RNA polymerase of a virus in a mammalian cell infected with the virus and/or if it is more efficient than antisense oligonucleotides at inhibiting expression of a viral RNA polymerase. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See ***KSR v. Teleflex***, 550 U.S. 398, 127 S. Ct. 1727 (2007).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '697 taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of a lentivirus. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '697 taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of an immunodeficiency virus. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '697 taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of a virus, wherein the gene is in an exon. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus by targeting the exon.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '697 taken with Cowsert, namely to produce an isolated mammalian cell comprising liposome or viral particle comprising a construct comprising a structural gene encoding RNA polymerase of a virus. One of ordinary skill in the art would have been motivated to combine the teaching since both are commonly used by one of ordinary skill in the art to successfully deliver a nucleic acid to a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 158-202 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,573,099 (of record) in view of Cowsert et al. (US 5,580,767, of record). Claims 1-5 of '099 recite:

> 1. An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence, wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, and wherein said at least two copies of said structural gene sequence are placed operably under the control of

a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of said promoter sequence.

2. An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence wherein each copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence.

3. An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence, wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, and wherein said at least two copies of said structural gene sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of said promoter sequence and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of said promoter sequence.

4. An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence and each copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence.

5. An isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural

> gene sequence, wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, and wherein said at least two copies of said structural gene sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of said promoter sequence, wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of said promoter sequence, and wherein said at least one copy of said structural gene sequence that is placed in the sense orientation relative to said promoter and said at least one copy of said structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.

The claims of ‘099 also recite an animal cell comprising the construct and method of using the construct.

However, the claims of ‘099 do not specifically teach a target gene selected from viral DNA polymerase, viral RNA polymerase, or a viral coat protein.

At the time the invention was made, Cowsert teaches an oligonucleotide for inhibiting RNA polymerase to reduce the proliferation of a virus (column 3). It is acknowledged that Cowsert is directed to making and using a nucleic acid inhibitor possibly with a different mechanism of inhibiting/reducing expression of a gene, then the mechanism for double stranded construct as claimed by Graham. Thus, one of ordinary skill in the art would have been obvious to try using the target gene for other nucleic acid inhibitors and studying whether there is an improvement using dsRNA compared to known nucleic acid inhibitor against the target gene.

In addition, at the time the invention was made, viral DNA polymerase and viral coat proteins were known to one of ordinary skill in the art for initiation of the disease or pathology of a virus. This would lead one of ordinary skill in the art to select a target

gene selected from a viral pathogen, e.g., virus comprising a viral DNA polymerase, viral RNA polymerase, or a viral coat protein because these genes are required for initiation of pathology. Thus, one of ordinary skill in the art could make a construct comprising a nucleotide sequence targeting expression of a viral polymerase with a reasonable expectation of success.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of the claims of '099 taken with Cowsert et al., namely to produce and use the claimed product. One of ordinary skill in the art would have been motivated to combine the teaching to study the inhibition of expression of a viral RNA polymerase of a virus in a mammalian cell infected with the virus and/or if it is more efficient than antisense oligonucleotides at inhibiting expression of a viral RNA polymerase. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See ***KSR v. Teleflex***, 550 U.S. 398, 127 S. Ct. 1727 (2007).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '099 taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of a lentivirus. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '099 taken with Cowsert,

namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of an immunodeficiency virus. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '099 taken with Cowsert, namely to produce an isolated mammalian cell comprising a construct comprising a structural gene encoding RNA polymerase of a virus, wherein the gene is in an exon. One of ordinary skill in the art would have been motivated to combine the teaching to improve and/or study the efficiency of inhibiting the virus by targeting the exon.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '099 taken with Cowsert, namely to produce an isolated mammalian cell comprising liposome or viral particle comprising a construct comprising a structural gene encoding RNA polymerase of a virus. One of ordinary skill in the art would have been motivated to combine the teaching since both are commonly used by one of ordinary skill in the art to successfully deliver a nucleic acid to a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 158-202 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 225-294 of

copending Application No. 10/346,853. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set claims read on a similar double stranded DNA construct and method of using the construct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 158-202 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 172-179, 181-186, 188, 190-193, 195-197, 199, 200, 202-205, 207-209, and 211 of copending Application No. 10/759,841. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set claims read on a similar double stranded DNA construct and method of using the construct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 158-202 are directed to an invention not patentably distinct from claims 1-22 of commonly assigned US Patent 6,573,099. Specifically, for the reasons set forth under the double patenting heading.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US Patent, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned

case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number 571-272-0764. The examiner can normally be reached on Monday-Thursday from 6:30 to 4:00 (Eastern Standard Time). The examiner can also be reached on alternate Fridays.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor Heather Calamita can be reached on 571 272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Brian Whiteman/

Primary Examiner, Art Unit 1635